Journal of the Saudi Society of Dermatology & Dermatologic Surgery (2011) **15**, 33–36

King Saud University

Journal of the Saudi Society of Dermatology & Dermatologic Surgery

www.ksu.edu.sa
www.jssdds.org
www.sciencedirect.com

CASE REPORT

Bilateral nevus of Ota associated with Turner syndrome

Fahad Alsaif *, Hissah Alshahwan

Department of Dermatology, King Khalid University Hospital, King Saud University, Riyadh, Saudi Arabia

Received 10 September 2010; accepted 20 September 2010
Available online 30 December 2010

KEYWORDS

Nevus of Ota;
Turner syndrome;
Saudi Arabia

Abstract In 1939, Ota described the first case of a benign dermal melanocytosis known as nevus of Ota. This condition involves the skin and mucosa innervated by the ophthalmic, maxillary and, rarely, the mandibular division of the trigeminal nerve. It is frequent in people of Japanese descent but is also seen in individuals of Chinese, Indian, African and European descent. Nevus of Ota is non-hereditary pigmentation disorder, which is more frequent in females than males. Unilateral presentation is typically seen, but bilateral involvement is described in 5–10% of patients. We report a 10-year-old Saudi girl with bilateral nevus of Ota associated with Turner syndrome. This is the first report of such an association.

1. Case report

A 10-year-old Saudi girl with a known case of Turner syndrome [chromosomal analysis, 46, X, del (X) (p22)] with growth hormone deficiency presented to the dermatology clinic with an asymptomatic blue-gray lesion on the upper part of the face that had been present since the age of 6 months. The lesions gradually progressed with age and extended to the forehead, temple and bilateral periorbital areas. They have been static for 5 years. There was a history of lesion darkening coincidence with growth hormone treatment. Her parents were non-consanguineous, and no one else in the family had similar pigmentation. Physical examination revealed a short stature and the subtle facial features of Turner syndrome. Cutaneous examination revealed a bilateral, diffuse, homogenous, slate-colored, blue-gray patch over the forehead, periorbital area, temples, nasal bridge and sclerae (Figs. 1 and 2). Nasal and oral mucosae were not affected. Other Turner syndrome features, including wide spaced nipples and wide carrying angle, were also present.

Ophthalmologic examination revealed scleral and *conjunctival pigmentation*, nystagmus and esotropia. Cardiologic and audiometric examinations were normal. Renal and ovarian ultrasounds were normal. Histopathologic study showed normal epidermis and the presence of numerous elongated, spindle-shaped melanocytes with their long axis parallel to the skin surface and scattered between the collagen bundles in the mid-dermis (Figs. 3 and 4).

Based on clinical findings and the complementary examinations performed, the diagnosis of Turner syndrome associated

* Corresponding author. Address: Department of Dermatology, P.O. Box 2925, Riyadh 11461, Saudi Arabia. Tel.: +966 1 4691427/26; fax: +966 1 4691432.
E-mail address: fsaif1000@hotmail.com (F. Alsaif).

Peer review under responsibility of King Saud University.
doi:10.1016/j.jssdds.2010.10.007

Production and hosting by Elsevier

Figure 1 Side view of the face showing diffuse slate – bluish-gray patch forehead, periorbital area and temple (eyes open).

Figure 2 Side view of the face showing diffuse slate – bluish-gray patch forehead, periorbital area and temple (eyes closed).

Figure 3 AP view shows bilateral nevus of Ota with bilateral scleral involvement.

with nevus of Ota was made in this patient. The patient is currently undergoing treatment with the *Q*-switched alexandrite laser with 755 nm wavelength, 3 mm spot size, and 7 J/cm^2 (see Fig. 5).

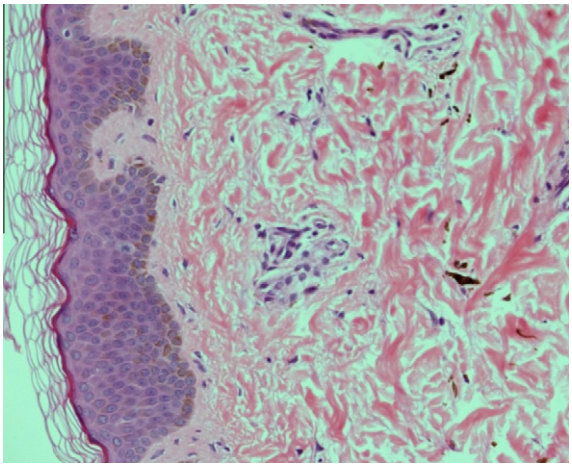

Figure 4 Skin biopsy show normal epidermis, dermis shows multiple spindle shaped melanophages lying with their long axis parallel to the skin surface and scattered between the collagen bundle in the mid-dermis, unremarkable subcutis (haematoxylin and eosin ∗ 200).

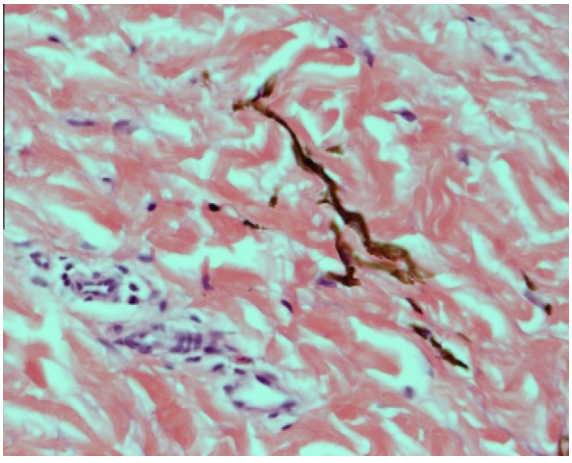

Figure 5 Skin biopsy shows dermal multiple spindle shaped melanophages lying with their long axis parallel to the skin surface and scattered between the collagen bundle in the mid-dermis (haematoxylin and eosin ∗ 400).

2. Discussion

Nevus of Ota was first described by a Japanese dermatologist, Ota, who described an unusual syndrome of Nevus fusco-caeruleus ophthalmo-maxillaris in 1939 (Ota, 1939a,b). It is very common in Asians, especially in the Japanese population, but is also seen in people of Chinese, Indians, African and European descent. Several epidemiological studies have shown higher prevalence in Japan with rates between 0.4% and 1.1% (Yoshida, 1952; Tanino, 1939; Hidano et al., 1967). A Canadian study in Black populations revealed an incidence of up to 0.014% (Gonder et al., 1982). About 80% of the patients were females (Kopf and Weidman, 1962). Forty-eight percent of patients developed a nevus of Ota at or after birth compared to 11% between 1 and 10 years of age and 36% at puberty

Table 1 Types of nevus of Ota.

Type I	(A) Mild orbital type: distribution over the upper and lower eyelids, periocular and temple regions (B) Mild zygomatic type: pigmentation is found in the infrapalpebral fold, nasolabial fold and the zygomatic region (C) Mild forehead type: involvement of the forehead alone (D) Involvement of ala nasi alone
Type II	Moderate type: distribution over the upper and lower eyelids, periocular, zygomatic, cheek and temple regions
Type III	The lesion involves the scalp, forehead, eyebrows and nose
Type IV	Bilateral type: both sides are involved

(Hidano et al., 1967). The pathogenesis of Ota's nevus is likely multifactorial, including genetic factors, as the lesion has a much higher incidence among Asians than in other populations (Loche and Bazex, 1999). Other stimulus factors are female sex hormones, ultraviolet light exposure and trauma (Kopf and Weidman, 1962). Histopathology of affected skin shows the presence of a benign dendritic melanocytosis containing melanin in the dermis (Kishikawa et al., 1997). The clinical manifestations are usually unilateral, and only 5% of cases are bilateral (De Las Heras et al., 1991). Presentation is characterised by the presence of blue-gray macular pigmentation with irregular borders and commonly involves skin and mucosa innervated by the ophthalmic, maxillary and rarely mandibular division of the trigeminal nerve (De Las Heras et al., 1991). Tanino classified nevus of Ota into four types, depending on the extent and distribution of pigmentation (Tanino, 1939), and according to this classification, this case would correspond to type IV (see Table 1).

Apart from skin and scleral involvement, pigmentation has been documented in the episclera, conjunctiva, cornea, iris, retina and uveal tract. Similar discoloration can be observed in oral and nasal mucosae and the tympanic membrane. Leptomeninges can also be affected (Patel et al., 1998). Open-angle glaucoma (Liu and Ball, 1991) and melanoma (Fulk and Morristown, 1984; Hartmann et al., 1981; Koca et al., 1992) are rarely associated with nevus of Ota with only about 10 cases of cutaneous melanoma in nevus of Ota documented to date. Melanoma arising in the brain and optical structures are more frequently associated with this type of lesion (Patel et al., 1998; Theunissen et al., 1993).

Turner syndrome is a sex chromosome disorder with an incidence between 1:2000 and 1:5000 live female births (Hook and Warburton, 1983; Gibbs et al., 2001). The defining clinical triad of impaired sexual development and webbed neck was first described in the English-language literature by Turner (1938), and later ovarian failure and streaked gonads were noted by Wilkins and Fleischmann (1944). The main features of this syndrome are short stature, impaired sexual development, infertility, webbed neck and lymphedema. Turner syndrome has been associated with many coincident cutaneous dermatoses. Although most patients with Turner syndrome have an increased number of acquired melanocytic nevi (Becker et al., 1994; Zvulunov et al., 1998), it is still unclear if this predisposes these individuals to melanoma, as it does in the rest of the population, or if Turner syndrome has some protective effect against melanoma (Schoemaker and Swerdlow, 2008; Gibbs et al., 2001). Because many case reports of melanoma have been reported with nevus of Ota, the risk of melanoma in our case needs to be considered. Other cutaneous associations with Turner syndrome are halo nevus (Oiso et al., 2007), vitiligo (Lowenstein et al., 2004; Hatipoglu and Kutoglus, 2000), neurofibromatosis (Lee and Yoo, 1996), lymphoedema (Rosina and Segalla, 2003), alopecia areata (Rosina and Segalla, 2003; Yang et al., 1996) and psoriasis (Yang et al., 1996; Lowenstein et al., 2004).

Various therapies have been used to treat nevus of Ota successfully. Cosmetic cover-up products can be used for camouflage. Cryosurgery and microsurgical treatments can leave disfiguring scars and are not recommended. Combined dermabrasion and carbon dioxide lasers have yielded good results (Shinichi and Hisahi, 1994). Treatment with photothermolysis with *Q*-switched lasers is safe and effective for lightening nevi of Ota (Omprakash, 2002; Chan et al., 2000; Kono et al., 2001). Side effects such as mild purpura, erythema and edema can follow the treatment and resolve after a few days, but pigmentation changes, such as hyperpigmentation or hypopigmentation, are more frequent. Topical tretinoin, hydroquinone, and corticosteroid creams can be used in the treatment of post-inflammatory hyperpigmentation (Ueda et al., 2000; Lu et al., 2000). The response to laser treatment has been reported to be dependent on lesion color. Darker lesions, which have a greater number of melanocytes, require more treatments for eradication (Chan et al., 2000). Overall, laser therapy is very effective in the treatment of nevus of Ota, and recurrence is rare (Omprakash, 2002; Ueda et al., 2000).

References

Becker, B., Jospe, N., Goldsmith, L.A., 1994. Melanocytic nevi in Turner syndrome. Pediatr. Dermatol. 11 (2), 120–124.

Chan, H.H., Leung, R.S., Ying, S.Y., Lai, C.F., Kono, T., Chua, J.K., Ho, W.S., 2000. A retrospective analysis of complications in the treatment of nevus of Ota with the *Q*-switched Alexandrite and *Q*-switched Nd:YAG lasers. Dermatol. Surg. 26 (11), 1000–1006.

De Las Heras, C., González, P., Manzano, R.M., Ferrer, M., Martín, M., Casado, M., 1991. Nevus de Ota bilateral. Actas Dermosifiliogr. 82, 245–247.

Fulk, C.S., Morristown, T.N., 1984. Primary disorders of hyperpigmentation. J. Am. Acad. Dermatol. 10, 1–16.

Gibbs, P., Brady, B., Gonzalez, R., Robinson, W., 2001. Nevi and melanoma: lessons from Turner's syndrome. Dermatology 202, 1–3.

Gonder, J.R., Ezell, P.C., Shields, J.A., et al., 1982. Ocular melanocytosis: a study to determine the prevalence rate of ocular melanocytosis. Ophthalmology 89, 950–952.

Hartmann, L.C., Oliver, G.F., Winkelmann, R.K., et al., 1981. Blue nevus and nevus of Ota associated with dural melanoma. Cancer 64, 182–186.

Hatipoglu, N., Kutoglus, S., 2000. Neurofibromatosis type 1 with overlap Turner syndrome and Klinefelter syndrome. J. Trop. Pediatr. 1, 3.

Hidano, A., Kajima, H., Ikeda, S., Mizutani, H., Niimura, M., 1967. Natural history of nevus of Ota. Arch. Dermatol. 95, 187–195.

Hook, E., Warburton, D., 1983. The distribution of chromosomal genotypes associated with Turner's syndrome: live birth prevalence rates and evidence for diminished fetal mortality and severity in genotypes associated with structural × abnormalities or mosaicism. Hum. Genet. 64, 24–27.

Kishikawa, T., Suzuki, T., Sasakia, Y., Aihara, K., Hirayama, T., 1997. Characterization of melanosomes and melanogenesis in cells cultured from Ota's nevus. J. Submicrosc. Cytol. Pathol. 29 (3), 339–352.

Koca, M.R., Rummelt, V.R., Fahlbusch, R., Naumann, G.O., 1992. Orbital, osseus, meningeal and cerebral findings in oculo-dermal. Melanocytosis (nevus of Ota). Clinico-histopathologic correlation in 2 patients. Klin. Monatsbl. Augenheilkd. 200, 665–670.

Kono, T., Nozaki, M., Chan, H.H., Mikashima, Y., 2001. A retrospective study looking at the long-term complications of *Q*-switched ruby laser in the treatment of nevus of Ota. Lasers Surg. Med. 29 (2), 156–159.

Kopf, A.W., Weidman, Al., 1962. Nevus of Ota. Arch. Dermatol. 85, 195–208.

Lee, W.S., Yoo, M.S., 1996. Alopecia areata in patient with Turner syndrome. Br. J. Dermal. 132 (6), 1013.

Liu, J.C., Ball, S.F., 1991. Nevus of Ota with glaucoma: report of three cases. Ann. Ophthalmol. 23, 286–289.

Loche, F., Bazex, J., 1999. Naevus de Ota. Ann. Dermatol. Venereol. 126, 745–748.

Lowenstein, E.J., Kim, K.H., Glick, S.A., 2004. Turner syndrome in dermatology. J. Am. Acad. Dermatol. 50 (5), 767–776.

Lu, Z., Chen, J., Wang, X., Fang, L., Jiao, S., Huang, W., 2000. Effect of *Q*-switched alexandrite laser irradiation on dermal melanocytes of nevus of Ota. Chin. Med. J. 113 (1), 49–52.

Oiso, N., Ota, T., Kawara, S., Kawada, A., 2007. Pustular psoriasis and vitiligo in patient with Turner syndrome. J. Dermatol. 34 (10), 727–729.

Omprakash, N., 2002. Treatment of nevus Ota by *Q*-switched, frequency doubled, ND:YAG laser. Indian J. Dermatol. Venereol. Leprol. 68, 94–95.

Ota, M., 1939a. Naevus fusco-caeruleus ophthalmomaxillaris. Jpn. J. Dermatol. 46, 369.

Ota, M., 1939b. Nevus fuscocoerulens ophtalmomaxillaris. Tokio Med. J. 63, 1243–1245.

Patel, B.C., Egan, C.A., Lucius, R.W., et al., 1998. Cutaneous malignant melanoma and oculodermal melanocytosis (nevus of Ota) report of a case and review of the literature. J. Am. Acad. Dermatol. 38, 862–865.

Rosina, P., Segalla, G., 2003. Turner syndrome associated with psoriasis and alopecia areata. J. Eur. Acad. Dermatol. Venereol. 17 (1), 50–52.

Schoemaker, M.J., Swerdlow, A.J., 2008. Cancer incidence in women with Turner syndrome in Great Britian: a national cohort study. Lancet Oncol. 9 (3), 239–246.

Shinichi, W., Hisahi, T., 1994. Treatment of nevus of Ota with the *Q*-switched Ruby laser. N. Engl. J. Med. 29 (331), 1745–1750.

Tanino, H., 1939. Naevus fusco-caeruleus ophthalmomaxillaris (Ota). Jpn. J. Dermatol. 46, 107–111.

Theunissen, P., Spincemaille, G., Pannebakker, M., Lambers, J., 1993. Meningeal melanoma with nevus of Ota: case report and review. Clin. Neuropathol. 12, 125–129.

Turner, H., 1938. A syndrome of infantilism, congenital webbed neck and cubitus valgus. Endocrinology 23, 566–578.

Ueda, S., Isoda, M., Imayama, S., 2000. Response of naevus of Ota to *Q*-switched ruby laser treatment according to lesion colour. Br. J. Dermatol. 142, 77–83.

Wilkins, L., Fleischmann, W., 1944. Ovarian agenesis: pathology, associated clinical symptoms and the bearing on the theories of sex differentiation. J. Clin. Endocrinol. 39, 204.

Yang, H.Y., Lee, C.W., Ro, Y.S., Yu, H.J., Kim, Y.T., Kim, J.H., Kim, J.H., 1996. *Q*-switched ruby laser in treatment of nevus of Ota. J. Korean Med. Sci. 11 (2), 165–170.

Yoshida, K., 1952. Naevus fusco-caeruleus opthalmo-maxillaris Ota. Tohoku J. Exp. Med. 55 (S1), 34–43.

Zvulunov, A., Wyatt, D.T., Laud, P.W., Esterly, N.B., 1998. Influence of genetic and environmental factors on melanocytic naevi: a lesson from Turner syndrome. Br. J. Dermatol. 138 (6), 993–997.